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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,048	01/28/2004	Nobuhiko Nomura	04853.0111	9606

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
09/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/765,048	NOMURA ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 6-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-5 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to the Amendment

The Amendment filed on 06/27/2007 in response to the previous Non-Final Office Action (3/27/2007) is acknowledged and has been entered.

Claims 1-12 are pending.

Claims 1-3 and 6-11 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 4-5 and 12 are currently under consideration.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Moreover, a translation of the copy of the JP 2003-21053 application is acknowledged and has been placed of record in the file.

Drawings

The petition filed under 37 CFR 1.84(a)(2)to accept color photographs is acknowledged and has been forwarded to the appropriate persons for their decision.

New Rejections Upon Further Consideration:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: how inhibition of Akt activity is being detected. In the instant case, it is unclear how Akt activity is being detected. For example, the detection step could reasonably interpreted as detecting Akt itself or alternatively, as detecting apoptosis which is an activity of Akt.

For examination purposes, detecting inhibition of Akt activity will be interpreted as detecting apoptosis or detecting caspase activity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pearson et al. (US 5,591,872, 1997, IDS) in view of Smith et al. (J. Immunol. 2001; 167; 366-374, IDS), Koo et al. (US 2002/0054869, 2002) and Rajan et al. (Am. J. Respir. Cell Mol. Biol. 2000; 23: 304-312).

Pearson et al. teach a method of selecting inhibitors of the autoinducer molecule, N-(3-oxododecanoyl) homoserine lactone, comprising contacting the autoinducer molecule with a suspected inhibitor, measuring the ability of the treated autoinducer molecule to stimulate the activity of a selected gene then determining whether the inhibitor represses or enhances the activity of the autoinducer molecule (column 5, lines 46-55). The patent further teaches a method of inhibiting the infectivity of *P. aeuriginosa* and methods of treating an immuno-compromised host infected by *P. aeruginosa*, e.g., a person afflicted with cystic fibrosis (column 6, lines 22-26).

Pearson et al. do not explicitly teach that the method comprising culturing animal cells with the test agent and acylated homoserine lactone and detecting the inhibition of Akt by detecting apoptosis.

Smith et al. teach a method of determining the affects of 3-O-C12- HSL (N-3-oxododecanoyl homoserine lactone) on MAP kinases, comprising contacting 16HBE cells with a test substance such as an inhibitor of the MAP kinase signaling pathway in the presence of 3-O-C12-HSL and determining the activation of ERK (page 371, 1st column, 1st full paragraph to 2nd column). In particular, the reference teaches that 3-O-C12-HSL activates the MAP kinase signaling pathway which is important in IL-8 production (page 371, 1st column, 1st full paragraph). Moreover, the reference teaches that 3-O-C12-HSL also induces NF-kB and AP-2 which subsequently upregulates

IL-8 which leads to neutrophil infiltration and inflammation found in P. aeruginosa infection (page 373, 2nd column, last paragraph). Lastly, Smith et al. teach that if structural analogs can be found that antagonize the ability of 3-O-C12-HSL to induce IL-8, they may prove useful therapeutically in cases where exuberant neutrophil responses lead to tissue injury.

Koo et al. teach that inhibition of the MAP kinase signaling pathway specifically triggers an apoptotic response in human cells (paragraph 0010). Koo et al. further teach that inhibitors of the MAP kinase signaling pathway such as PD9805 are useful for inhibiting the growth of a tumor in a mammal, wherein the inhibitor induces a cytotoxic response leading to apoptosis of cells in said mammal (Claims 16-20 of US 2002/0054769).

Rajan et al. teach the induction of apoptosis by *Pseudomonas aeruginosa* in respiratory epithelial cells. In particular, the reference teaches that the resistance of airway epithelial cells to apoptosis is due to the stimulation of NF-κB by adherent *P. aeruginosa*, wherein NF-κB appears to have an antiapoptotic effect in respiratory cells.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to culture a test substance in the presence of N-3-oxodocecanoyl homoserine lactone as taught by Pearson et al. in an animal cell such as a neutrophil and to identify an inhibitor of N-3-oxodocecanoyl homoserine lactone by detecting apoptosis in view of the teachings of Smith et al., Koo et al. and Rajan et al.. One would have been motivated to do so because Smith et al. teaches that 3-O-C12-HSL induces MAP kinases, as well as NF-κB, each of which are known in the art to be involved in apoptosis in view of the teachings of Koo et al. and Rajan et al.. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by culturing a test substance in the presence of N-3-oxodocecanoyl homoserine lactone as taught by Pearson et al. in an animal cell such as a neutrophil and to identify an inhibitor of N-3-oxodocecanoyl homoserine lactone by detecting apoptosis in view of the teachings of Smith et al., Koo et al. and Rajan et al., one would achieve an effective method of identifying a suitable inhibitor for the treatment of an immunocompromised host infected by *P. aeruginosa*, e.g., a person afflicted with cystic fibrosis.

Claims 4-5 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pearson et al. (US 5,591,872, 1997, IDS) in view of Telford et al. (Infection and Immunity, 1998; 36-42) and

Maianski et al. (Blood, 2002; 101: 1987-1995, prepublished online as Blood First Edition Paper, October 10, 2002).

Pearson et al. teach a method of selecting inhibitors of the autoinducer molecule, N-(3-oxododecanoyl)homoserine lactone, comprising contacting the autoinducer molecule with a suspected inhibitor, measuring the ability of the treated autoinducer molecule to stimulate the activity of a selected gene then determining whether the inhibitor represses or enhances the activity of the autoinducer molecule (column 5, lines 46-55). The patent further teaches a method of inhibiting the infectivity of *P. aeuriginosa* and methods of treating an immuno-compromised host infected by *P. aeruginosa*, e.g., a person afflicted with cystic fibrosis (column 6, lines 22-26).

Pearson et al. do not explicitly teach that the method comprising culturing animal cells with the test agent and acylated homoserine lactone and detecting the inhibition of Akt by detecting apoptosis or caspase activity.

Telford et al. teach that the *Pseudomonas aeruginosa* Quorum-Sensing Signal Molecule N-(3-Oxodocecanoyl)-L-homoserine Lactone has immunomodulatory activity and inhibits the production of tumor necrosis factor alpha by lipopolysaccharide-stimulated macrophages (abstract).

Maianski et al. teach that the mechanism of apoptosis induction by TNF-α is closely related to the cascade of apoptotic cysteine proteases known as caspases which represent a group of enzymes responsible for initiation and execution of apoptosis, wherein TNF-α induces apoptosis through the activation of caspases (page 1987, 1st column, 2nd full paragraph and page 1993, 2nd column, 2nd full paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to culture a test substance in the presence of N-3-oxodocecanoyl homoserine lactone as taught by Pearson et al. in an animal cell such as a neutrophil and to identify an inhibitor of N-3-oxodocecanoyl homoserine lactone by detecting apoptosis or caspases activity in view of the teachings of Telford et al. and Maianski et al.. One would have been motivated to do so because Telford et al. teaches that 3-O-C12-HSL inhibits TNF-α production which is well known in the art to be involved in apoptosis via the activation of caspases as taught by Maianski et al. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by culturing a test substance in the presence of N-3-oxodocecanoyl homoserine lactone as taught by Pearson et al. in an animal cell such as a neutrophil and to identify an inhibitor of N-3-oxodocecanoyl homoserine

lactone by detecting apoptosis or caspase activity in view of the teachings of Telford et al. and Maianski et al., one would achieve an effective method of identifying a suitable inhibitor for the treatment of an immuno-compromised host infected by *P. aeruginosa*, e.g., a person afflicted with cystic fibrosis.

Therefore, NO claim is allowed

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

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